GRADIVA

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

Early Detection of Parkinson's Disease Using Machine Learning: A Comprehensive Review

Pankaj V. Itkalkar[1] & Dr. Suresh C. Kuri[2]

1.Electronics and Communication Engineering Department, KLS Gogte Institute of Technology, Belagavi.
2.Associate Professor, Electronics and Communication Engineering Department,
KLS Gogte Institute of Technology, Belagavi.
Email: [1]pvi47@rediffmail.com, [2]sureshkuri@git.edu

Abstract

Parkinson's disease (PD) gradually impairs neural pathways responsible for motor control, leading to progressive functional decline. If it is not detected in early stage this may cause severe disability among patients with PD. Various machine learning (ML) techniques can be found useful tools in the analysis of various biomedical data to diagnose the PD in early stages. This literature review is a in detail survey of the existing approaches to ML models, data types which can be used, feature extraction, performance of various ML algorithm, and recent trends in this area. This paper mentions challenges, ethical issues, and future directions in the study of early detection of PD with multi-omics data and wearable sensor technologies. To develop precise ML models the importance is given for the validation of ML models and translation of clinical data using ML models.

Keywords: *Parkinson's Disease, Early Detection, Machine Learning, Neuroimaging, Biomarkers, Wearable Devices, Multi-Omics, Explainable AI, Federated Learning.*

1. INTRODUCTION

Parkinson's disease (PD) is a long-term, progressively worsening neurological condition that results from degeneration within specific regions of the central nervous system. Although motor impairment such as tremor, rigidity, and bradykinesia remains its most recognizable feature, the disorder is also associated with numerous non-motor manifestations affecting cognition, mood, sleep, and autonomic regulation. The condition was first systematically documented in 1817 by James Parkinson. From a neuropathological perspective, PD is characterized by the gradual loss of dopamine producing neurons located in the substantia nigra pars compacta, accompanied by the formation of Lewy bodies, intracellular inclusions composed predominantly of misfolded α-synuclein protein. [1].

There are some primary motor features like bradykinesia, tremor that appears when the limbs are at rest, muscle stiffness, and difficulties with balance and posture. These motor features usually become noticeable only after when 60–80% of dopamine producing neurons have been lost which is demonstrated in [2]. There are also some non-motor symptoms which can be seen years before motor symptoms emerge.

The non- motor symptoms include reduced sense of smell, gastrointestinal disturbances like constipation, REM sleep behaviour disorder, and mood changes including depression. The study done by W. Poewe et al. in [3] shown that these biomarkers are recognized as potential early markers of PD. Early identification of PD is essential for medications or behavioural therapy treatments if they started in the early stages of the disorder [4]. Moreover, to improve patients' overall quality of life timely diagnosis facilitates more effective long-term planning.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

Current diagnostic practices depend mostly on clinical observation. Although there is lack of reliable objective biomarkers, as a result diagnosing the disease is often delayed and sometimes an imprecise diagnosis is done during the initial phases of the disease [5].

As a result of these limitations, there has been an increased interest in using machine learning (ML) methods to aid in the early detection of Parkinson disease. ML models can handle multidimensional and large-scale data sets and can find subtle disease onset indicators which may have gone unnoticed by clinicians. Such techniques have been examined on various data modalities such as voice samples, handwriting analyses, gait features and neuroimaging data. [6], [7].

The following review paper is aimed at providing a general overview of ML based solutions to early PD detection. In this paper, the data sources that are usually used, the most common ML algorithms, the measures applied to test the performance of models, major findings of recent studies, and existing challenges and opportunities in the area are considered.

II. Early Parkinsonism Motor Symptoms

Motor impairment is still the clinical characteristic of the Parkinson disease (PD) and it is the core of its existing diagnostic criteria. The primary motor manifestations of Parkinson's disease include bradykinesia, resting tremor, muscular rigidity, and postural instability. These symptoms arise from dysfunction within basal ganglia circuits caused by the progressive loss of dopamine producing neurons in the substantia nigra. [9], [3].

Even though these manifestations are usually observed when relatively large neuronal damage has already taken place, there is a possibility of slight changes in the motor system being observed during the prodromal or early stage of the disease, which would provide potential sources of earlier diagnosis. Following are some motor symptoms discussed.

A. Bradykinesia

The slowing of voluntary movement is called bradykinesia. It is regarded as the most typical and crucial motor symptom of PD. It is presented in the form of low movement amplitude, hesitations, and inability to start or maintain repetitive movements. The first indicators may be looked at in the field of fine motor activity: finger tapping, writing, or clothes buttons [153].

B. Resting Tremor

Ranging in approximately 70 percent of the patients, rest tremor may begin on one hand or fingers. This is normally supported by free motion but it recurs again during rest. Although tremor is not consistently the earliest presenting symptom, it remains a key clinical indicator that often raises suspicion of PD [11].

C. Rigidity

Rigidity refers to an abnormal increase in resistance to passive limb movement that remains constant regardless of movement velocity. It may manifest itself as cogwheel rigidity and together with tremor. Early PD rigidity may be mild and manifested as stiffness in the neck or shoulders and is likely to be confused with musculoskeletal issues. In many cases, rigidity becomes more pronounced during voluntary movement of other body regions, a phenomenon commonly used to enhance the clinical detection of subtle or mild rigidity, as reported by Massano et al. [155].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

D. Postural and Gait Abnormalities

The postural instability typically becomes apparent later in the disease process. However, early on gait deviations including arm swing deficiency, shuffling, and turn around difficulty are evident at early stages. Wearable inertial measurement units (IMUs), pressure sensitive mats, which utilize instrumented gait analysis as a method have demonstrated observable changes in gait patterns prior to the manifestation of overt clinical symptoms [50], [30].

E. Objective Assessment Resources

In addition to clinical assessment, some of the digital and quantitative techniques have been used to identify minor motor changes in the early stage of PD. These are handwriting and spiral drawing, digitized finger tapping, speech based tests, and kinematic tests of gait and balance. The application of ML techniques to such datasets has demonstrated promising performance in distinguishing individuals with PD from healthy controls. [22], [159].

III. Early Parkinsonism Non Motor Symptoms

Although motor impairments constitute the main diagnostic characteristic of the PD, a wide range of non-motor symptoms is often revealed many years prior to the onset of the overt motor signs. Such symptoms represent the general participation of non-dopaminergic neurotransmitter mechanisms and extranigral areas of the brain. There is growing recognition of NMS as important in early diagnosis because they may be used as prodromal markers and make a significant contribution to quality of life [160], [161].

A. Olfactory Dysfunction

Hyposmia or anosmia is one of the most frequent prodromal alterations. It occurs in up to 90 percent of PD patients. The discriminatory capacity of PD patients vs controls has been demonstrated to be high with measured olfactory tests (e.g. the University of Pennsylvania Smell Identification Test (UPSIT)) and Sniffin Sticks [162]. Olfactory dysfunction may be utilized as an early biomarker because it may start showing decades before motor symptoms.

B. Sleep Disorders

Sleep disorders and sleep disturbances, especially the REM sleep behaviour disorder (RBD) have a strong correlation with a high probability of getting PD. RBD is characterized by the absence of normal muscle atonia during REM sleep, resulting in dream-enactment behaviours. Longitudinal analyses have shown that patients with idiopathic RBD are highly susceptible to Parkinson disease or other disorders of the 3-alpha-synuclein-related neurodegeneration [163]. The Polysomnography is the gold standard in the diagnosis of RBD, and the sleep tracker is a wearable device that begins to be used as a screening method.

C. Cognitive and Mood impairments

The frequent ones are mild cognitive impairment, depression, anxiety and apathy that can even exclude motor symptoms in the early PD. Montreal Cognitive Assessment (MoCA) is widely used neuropsychological tool to determine cognitive impairment. There is also high risk of development of PD associated with mood disorders [164].

D. Autonomic Dysfunction

The non-motor impairments are typically autonomic defects, including constipation, resistant urinary urgency, erectile dysfunction, and orthostatic hypotension. Gastrointestinal dysfunction, in particular constipation, can appear several years before motor symptoms appear

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

and it can be regarded as a powerful prodromal marker [165]. The objective measures are the heart rate variability (HRV) testing and testing the autonomic functioning.

E. Biological Markers

Several biological measures have been considered as potential early warning. The cerebrospinal fluid (CSF) biomarkers of total a-synuclein, tau, and 2-amyloid are not normally expressed in PD patients [166]. Additionally, presynaptic dopaminergic wasting can be detected by dopamine transporter imaging (DaT-SPECT) before clinical diagnosis and gives very persuasive evidence [167].

When combined with motor measures and computational tools, these non-motor characteristics, in totality, are not only informative, in respect to the multisystem nature of PD, but also can be useful as candidates of early diagnosis and risk stratification. To provide a comprehensive report of the studies conducted in the early detection of PD, in both motor and non-motor symptoms, a comparative structure has been put in a single summary. Motor aspects are vibration, walking, and speech pathology which have been continuously monitored with wearable sensors, voice information, and machine learning (ML) and had a high classification percentage. At the same time, non-motor ones like olfactory dysfunction, REM sleep behaviour disorder (RBD), cognitive and mood changes, autonomic disturbances, and biological markers also gained the same level of importance as early predictors and often motor manifestation is predetermined by years. The following table represents the results of the two domains, and shows the detection methods, datasets to use, the algorithm to use, predictive accuracy, and the studies that are the most relevant and indicate their ability to detect and track PD in its initial stages.

Table1: Summary of Motor and Non Motor Symptom Studies in Early PD

Symptom Type	Method of Detection	Dataset / Assessment Tool	ML Algorithm / Analysis	Accuracy / Predictive Value	Key Study (Ref.)
Motor – Tremor	Accelerometers, gyroscopes	Smartphone & wearable sensor data	SVM, RF	>85% classification accuracy	Arora et al., 2015 [181]
Motor – Gait	Pressure sensors, instrumented mat (GAITRite)	GAITRite; 303 participants (119 PD, 184 HC)	Random Forest (with information gain & RFE), SVM, logistic regression	97 % accuracy with features selected with RFE SVM	Rehman et al., 2019 [182]
Motor – Speech	Acoustic feature extraction (voice)	UCI Parkinson's dataset (voice data)	SVM	~92% accuracy with sustained phonation tasks	Trabassi et al, 2022 [30]
Non Motor – Olfaction	Smell identification tests	UPSIT, Sniffin' Sticks	Statistical classification	Hyposmia in >80% of early PD cases	Haehner et al., 2011 [162]
Non Motor – Sleep (RBD)	Polysomnography, sleep questionnaires	PSG, RBDQ	Longitudinal predictive modeling	>70% conversion to PD/α synucleinopathy in 10 yrs	Postuma et al., 2012 [163]
Non Motor – Cognition	Neuropsychological testing	MoCA, MMSE	Statistical correlation, ML	Early deficits predict faster PD progression	Per et al., 2012 [164]
Non Motor – Mood	Depression/anxiety rating scales	BDI, HAM-D	Regression & predictive modeling	Depression may precede motor symptoms	Weintraub & Burn, 2011 [161]
Non Motor – Autonomic	GI motility tests, HRV analysis	Clinical & physiological datasets	Statistical analysis, ML	Constipation >10 yrs before motor onset; HRV loss early	Schapira et al., 2017 [165]
Non Motor – Biomarkers	CSF analysis	α-synuclein, tau, β-amyloid	Logistic regression, ML classifiers	Altered CSF profile distinguishes PD from controls	Hana et al., 2010 [166]

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

Non Motor – Imaging	Molecular imaging	DaT-SPECT	Imaging based classifiers	Detects presynaptic dopamine loss preclinically	Brooks, 2010 [167]

IV. Neuroimaging and Neurophysiological Biomarkers

Neuroimaging and neurophysiological biomarkers have turned out to be key player in the hunt of early diagnosis of the Parkinson disease (PD). It provide objective evidence of structural, functional and biochemical alteration that precedes or is correlated with the clinical manifestations. Unlike clinical measures, these modalities permit observation of the pathology of the underlying disease, distinguish among other movement disorders, and, in clinical trials, can serve as a surrogate endpoint [3].

A. Structural MRI

Feraco, Paola et al in [171] demonstrated that structural magnetic resonance imaging (MRI) has become popular to detect atrophy and microstructural changes in PD. Conventional MRI may be found normal in the initial stages of the disease; however, some advanced imaging techniques such as voxel-based morphometry (VBM) and diffusion tensor imaging (DTI) have been used to demonstrate subtle changes in the substantia nigra, basal ganglia and the cortical regions [171]. These alterations are linked with motor and cognitive impairment and might represent non-invasive predictors of early pathology.

B. Functional MRI (fMRI)

The disrupted functional interrelationships in brain networks are provided through functional MRI. It has also been demonstrated by resting state fMRI studies that there is compromised connectivity of cortico striatal networks and cortico cerebellar networks in early PD due to compensatory mechanisms and dysfunctional disease [172]. Task based fMRI is also known to identify abnormal patterns of activation during both motor and cognitive activities that can be differentiated in PD patients and healthy controls.

C. Positron Emission Tomography (PET) and SPECT Imaging

Molecular imaging techniques which can be used to observe dopaminergic deficit prior to the development of motor symptoms include PEET and single photon emission computed tomography (SPECT). Dopamine transporter (DaT) SPECT has particularly been useful in the differentiation between PD and essential tremor and atypical Parkinsonism [173]. Dopamine synthesis (e.g. [18F] DOPA) and glucose metabolic (FDG PET) tracers of PET are quantitative measures of striat dysfunction and network remodelling [174].

D. Neurophysiological Markers

Electrophysiological methods are also accepted as biomarkers of PD. In these methods electroencephalography (EEG), magnetoencephalography (MEG), and transcranial magnetic stimulation (TMS) are included. Unusual EEG oscillatory activity in the beta frequency range is related with motor dysfunction. Whereas TMS can quantify cortical excitability and plasticity that modulate at an initial phase of the disease [175]. They are less expensive and more commonly more accessible than imaging and can be incorporated into multimodal diagnostic models together with neuroimaging.

E. Integration with Machine Learning

Recent literature is now applying machine learning to neuroimaging and neurophysiological data. By using ML approach to these data it can be possible to identify

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

subtle features impossible to identify by humans. As an example, convolutional neural networks (CNNs) trained on MRI or PET image have been shown to be highly accurate in classifications of mechanisms of PD patients as compared to controls and predicting disease progression [176].

The predictive performance can be enhanced further by integrating imaging modalities with the non-motor clinical data. This fact highlights the significance of multimodal integration in early detection strategies.

Table 2: Summary of Neuroimaging and Neurophysiological Biomarker Studies in Early Parkinson's Disease

Biomarker Type	Modality / Method	Dataset / Tool	ML / Analysis Approach	Accuracy / Predictive Value	Key Study (Ref.)
Structural Changes	MRI (VBM, DTI)	Multicenter clinical cohorts	Statistical + ML classifiers	Subtle atrophy in substantia nigra and basal ganglia detectable in early PD	Feraco, Paola et al., 2021 [171]
Functional Connectivity	Resting state & task based fMRI	Parkinson's patient fMRI datasets	Network analysis, ML (SVM, RF)	Altered cortico striatal and cortico cerebellar connectivity; predicts motor decline	Tahmasian et al., 2017 [172]
Dopaminergic Deficits	DaT SPECT	PPMI & clinical imaging datasets	Imaging based classifiers	Differentiates PD from essential tremor with high sensitivity/specificity	Brooks & Pavese, 2020 [173]
Metabolic Activity	FDG PET, [^{18}F] DOPA PET	PPMI, hospital PET imaging cohorts	CNNs, logistic regression	Detects striatal hypometabolism and dopamine loss preclinically	Politis, 2014 [174]
Electrophysiological Oscillations	EEG, MEG (beta band power, coherence)	Clinical EEG/MEG recordings	Signal processing, ML (SVM, DL)	Abnormal beta activity linked to early motor symptoms	Waninger, Shani et al., 2020 [175]
Cortical Excitability	Transcranial Magnetic Stimulation (TMS)	Clinical neurophysiology labs	Statistical analysis	Reveals altered excitability and plasticity in early PD	Waninger, Shani et al., 2020 [175]
Multimodal Imaging + ML	MRI + PET + clinical data	PPMI, ADNI, local hospital datasets	CNNs, hybrid deep learning models	>90% accuracy in PD classification, improved prediction of progression	Li et al., 2020 [176]

The recent developments highlight the importance of integrating neuroimaging and neurophysiological techniques with machine learning. These developments positively contribute to the early detection of PD. MRI and PET can show evidence of structural and functional evidence of dopaminergic degeneration in neuroimaging and EEG. TMS can capture the first signs of neurophysiology changes that cannot necessarily be seen using imaging alone.

Multimodal fusion (MRI, PET, clinical features, etc.) based models have always shown high predictive accuracy, and better modeling disease progression, compared to other single modality models [171][176].

This convergence of neuroimaging and electrophysiology with ML can not only enhance the precision of the diagnosis but also offer the pathway to objective biomarkers of tracking a disease and determining therapeutic effects to patients on an individual basis.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

2. CHALLENGES IN EARLY DIAGNOSIS OF PD AND THE ROLE OF ML

PD is a clinical neurological issue. It has been difficult to diagnose in early stages. The difficulty to diagnose in early stage is caused by a variety of interrelated factors:

2.1 Diagnostic Limitations in Early Stages

In the early stages of PD the symptom are usually mild, non-specific and looks similar to other neurodegenerative illness such as essential tremor or drug induced Parkinsonism. There are various diagnostic criteria of PD exists. These are the UK Parkinson's Disease Society Brain Bank criteria and MDS Clinical Diagnostic Criteria. These diagnostic criteria largely depend on motor symptoms observation. But motor symptoms occur only after the large scale loss of dopaminergic neurons [5], [9].

There is also no conclusive laboratory or imaging test of PD. Only supportive tool in the form of DaTscan (dopamine transporter imaging) is available. But it is costly, not widely distributed and not differentiated among different syndromes of Parkinsonism, It may be used to aid diagnosis only [9]. D. Hughes et at. used clinical assessment and neuropathological examination on 100 patients. The clinical accuracy diagnosis of Parkinson's disease (PD) in this study was approximately 80%. But the number of misdiagnoses cases may be as high as 18 percent at the initial stages of disease [11].

2.2 Heterogeneity of Symptoms

PD is very heterogeneous in aspects of its clinical presentation and progression. Patients can either show up with tremor dominant symptoms or others can show up with postural instability and gait disturbances as the predominant ones (PIGD). In addition, there are non-motor symptoms (sleep disturbances, olfactory dysfunction, depression, and cognitive impairment) that may manifest several years prior to motor symptoms, which makes it difficult to detect them early [3].

2.3 Lack of Robust Biomarkers

Several of the possible biomarkers have been studied, including neuroimaging data, cerebrospinal fluid proteins, and genetic profiles, but none of these has so far been used clinically in the context of early diagnosis [13]. Sensitive and specific biomarkers are not available and this leads to delays in correct diagnosis and treatment of PD.

2.4 Addressing Diagnostic Challenges with Machine Learning

Machine learning (ML) is one of the most promising solutions to eliminate such diagnostic drawbacks. ML has the potential to reveal low level patterns and interactions between clinical, physiological, and behavioural variables that are difficult to detect using conventional statistical techniques, by making use of computational models capable of learning high dimensional, complex data.

Advantages of ML in early PD detection:

- **Multimodal data integration:** Different data types are available such as voice records, handwriting dynamics, gait recordings, wearable sensor recordings, neuroimaging, and genetic data. ML models can be trained with these different data types which help to improve diagnosis of disease. [14], [15].
- **Dimensionality reduction and feature selection:** The most helpful features from datasets may be selected and ranked using the ML algorithms to be used in diagnosis. This will

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

enhance precision in the absence of over fitting. Random Forests, Least Absolute Shrinkage and Selection Operator (LASSO), Principal Component Analysis (PCA), etc.) are some of the dimension reduction algorithms that can be used.

- **Early symptom recognition:** Deep learning models (e.g., CNNs, RNNs) and supervised models (e.g., SVMs, Decision Trees) and can be used effectively to identify preclinical signs of PD during prodromal stages. [17], [18].
- **Scalability and real time application:** Scalable solutions can be provided by using ML models. The ML models can be integrated into a mobile health application or telemedicine environment and trained to assist in enhancing access to early screening solutions.

There are several benefits of applying ML models in the process of detecting PD. The challenge of validation of large and heterogeneous datasets creates significant difficulties to ML models. ML models cannot be validated but need to be validated in large and diverse populations to make their generalizability and clinical reliability.

3. DATA MODALITIES USED IN ML FOR PD DETECTION

Parkinson disease ML models are sensitive to the type, quality and quantity of input data. Various data modalities have been used to quantify different phenotypes of PD pathology and symptomology. Neuroimaging, voice records, movement data, and biological records are the most common sources of data. Each of these two types of data possesses its insights and can be useful in creating effective and powerful predictive models.

3.1 Neuroimaging Data

Neuroimaging modalities consist of structural MRI, functional MRI (fMRI), PET, and DaTscan. These are often utilized to image both anatomical and functional changes in the brain after PD. It is possible to detect atrophy in regions such as the substantia nigra and basal ganglia with structural MRI. But functional connectivity and dopaminergic activity can be identified with fMRI and PET scans [19].

The ML models that have been successfully used to learn useful features in high dimensional neuroimaging data are support vector machines (SVMs), convolutional neural networks (CNNs) and auto encoders.[20], [29], [32] Studies that have used those procedures have reported classification rates higher than 85 percent between PD patients and healthy controls [38], [39].

However, the high cost and inefficient supply of neuroimaging equipment threatens the wide adoption of this type of models, particularly in under resource settings.

3.2 Voice and Speech Recordings

PD is described as having speech abnormalities. There are various features of speech like low vocal intensity, monotone vocal style and inaccurate articulation. This can precede motor symptoms by several years. In general, voice recordings are used to derive acoustic features such as pitch variation, shimmer, jitter and HNR are helpful biomarkers [21], [22].

Examples of ML algorithms that have yielded promising results when it comes to classifying PD, using voice features include random forests, logistic regression and deep neural networks. The modality, in particular, has potential in the implementation of scalable screening applications with mobile or telehealth.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

3.3 Movement and Gait Data

The motor impairments in PD are varied and may include motions that shake, become rigid, slow, cannot move, and lose balance. Complex movement data can be detected with wearable devices (e.g., accelerators, gyroscopes, inertial measurement units) and smartphone apps when someone is walking, making gestures with their hands, or performing other motor activities [23].

These movement and gait data signals are analysed. Properties such as stride length, step variability, tremor frequency and acceleration patterns are extracted. Such extracted features have been applied to various ML models such as supervised learning methods, including decision trees, SVMs, and deep learning models for the early detection and monitoring of Parkinson's [24]. A movement data are also very useful as they can be created in a non- invasive way, regularly and in naturalistic environments.

3.4 Dynamics in Handwriting and Drawing

A lack of fine motor control in handwriting and micrographia (abnormally small handwriting) is a symptom of PD. There are some kinematics properties which can be useful as PD detection features like writing speed, writing pressure, and smoothness of the strokes. These kinematic properties and the temporal (digitized samples of handwriting, e.g. spiral tests, sentence writing) can be measured using graphic tablets [25].

Such data is used by ML models to identify the initial symptom of motor degradation. Several studies provide a high classification rate of CNNs and recurrent neural networks (RNNs) on handwriting data [26].

3.5 Biological and Genetic Biomarkers

Biological markers that are used in PD research are alpha-synuclein, the level of dopamine transporter, and the elements of cerebrospinal fluids (e.g., tau and beta-amyloid) due to their potential application in the disease diagnosis at an early stage. Besides, LRRK2, PARK7, SNCA and GBA genetic mutations are found to cause heightened risk of PD [27].

Despite the potential of these biomarkers, they are in the early discovery phase of being used in ML models because there is a very limited amount of data and standardization is also an issue. Still, the future of multimodal ML models is the inclusion of biomarker data with either behavioural or imaging phenotype [28].

Table 3: Common Publicly Available Datasets for PD Machine Learning Research

Modality	Dataset Name	Data Type	Description	Source / URL
Voice	UCI Parkinson's Dataset	Acoustic voice measurements	195 voice recordings from 31 patients	UCI ML Repo
	Parkinson's Telemonitoring Dataset	Speech features + clinical data	5,875 daily voice samples from 42 patients	UCI ML Repo
Movement/ Gait	Daphnet Freezing Gait Dataset	Wearable accelerometer data	Detect freezing of gait episodes in PD patients	Daphnet
	mPower Dataset	Smartphone sensor + survey data	Gait, tapping, and voice data from thousands of users	Synapse
Handwriting	Spiral Dataset (HandPD)	Digitized drawing tasks	Spiral test data collected using digital tablets	Often referenced in [Pereira et al., 2021] [26]
Neuroimaging	PPMI	MRI, DaTscan, CSF, genetics	Comprehensive longitudinal biomarker rich PD cohort	PPMI

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

Multi modal	Gait in PD Dataset	Video + IMU + pressure sensors	Multimodal gait recordings for PD classification	PhysioNet
	Neurocon Biomarker Dataset	EEG + clinical + cognitive	Biomarkers for PD and Alzheimer's detection	Neurocon

Note: Some datasets (like PPMI or mPower) may require registration and data use agreements due to privacy concerns.

4. ML ALGORITHMS IN PD DETECTION

Various types of ML algorithms were developed and deployed to identify Parkinson's disease in different data modes. Depending upon the nature of i/p data and feature engineering, these tools may be more or less complex, interpretable, and high performance. This section is a summary of the most common ML algorithms which includes SVMs and the RFs and deep learning models.

4.1 Support Vector Machines (SVM)

- SVMs are one of the most commonly used classifiers in the study of Parkinson disease (PD). They are effective when dealing with high dimensional feature spaces and small sample sizes. The principle of SVM is to find an optimal hyperplane distinguish between data points of different classes with maximum possible margin and thus improves the generalization.
- **Applications**: SVMs are used in a wide variety classification of PD related tasks. Some of the applications include speech based identification, neuroimaging based classification, and motion pattern identification.
- **Advantages**: SVMs are best suited for classification of high dimensional feature spaces and small sample sizes.
- **Limitations**: Performance of SVM is affected due to noise present in the dataset. Also the choice of kernel parameters requires careful tuning.
- **Example:** Tsanas et al. showed over 92 percent accuracy with voice data and SVMs on the UCI Parkinson data [22].

4.2 Random Forests (RF)

Random Forest is an ensemble algorithm. It creates many decision trees throughout the training process. It then combines their predictions through a majority vote to find the final classification.

- **Applications:** RF has been extensively applied in gait analysis, sensor based features, and multimodal data.
- **Advantages:** RF algorithms can be extensively used with nonlinear relationships. They are used in reduced overfitting and can be interpreted as feature importance. Big forests may be computer and memory intensive.
- **Limitations**: Large forests are very computationally and memory intensive.
- **Example**: As demonstrated by Trabassi et al. (2022), Random Forest, SVM and Decision Tree classifiers attained more than 80 percent accuracy on distinguishing PD patients and healthy controls based on gait features captured by a wearable IMU sensor. [30].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

4.3 Artificial Neural Networks (ANN)

ANNs are based on biological neural networks and are composed of layers of connected nodes that convert input attributes into outputs by summing weights and activation functions.

- **Applications:** Voice feature classification, movement detection based on the accelerator data and forecasting the clinical symptoms.
- **Advantages:** Can be used to model complicated non-linear relationships, flexible architectures.
- **Limitations:** Require more data, prone to over fitting without regularization.

Example: Little et al. deployed a feed forward neural network to speech characteristics to monitor the development of PD at high accuracy levels [31].

4.4 Deep Learning Approaches

Convolutional Neural Networks (CNNs), Recurrent Neural Networks (RNN), and Long Short Term Memory (LSTM) networks are increasingly gaining applications in the PD diagnosis. These deep learning models are capable of learning hierarchical representations using raw or minimally processed data.

Convolutional Neural Networks (CNN)

- **Applications:** CNNs are used in Neuroimaging (e.g., MRI, DaTscan), handwriting (spiral test), and video gait analysis.
- **Strengths:** CNNs are excellent at feature extraction from spatial data. They often used for image or spatial signal classification.
- **Limitations:** Require large datasets and significant computational resources.
- **Example:** Pereira et al. applied a CNN to classify spiral drawing samples from PD patients, achieving 94% accuracy [26].

Recurrent Neural Networks (RNN) and LSTM

- **Applications:** RNN and LSTM are used in time series data such as speech signals, gait dynamics, and wearable sensor data.
- **Strengths:** RNN and LSTM can capture temporal dependencies and sequential patterns.
- **Limitations:** Having training complexity, vanishing gradient problem in RNNs (mitigated in LSTMs).
- **Example:** Trabassi et al. applied LSTM networks to smartphone based gait data and achieved high diagnostic accuracy [30].

Table 4: Comparative Summary

Algorithm	Best Suited For	Strengths	Limitations
SVM	Voice, imaging, small datasets	High accuracy, good generalization	Kernel selection, interpretability
Random Forest	Sensor, clinical, multimodal	Feature ranking, low over fitting	Less effective with sparse data
ANN	Voice, movement	Models nonlinear patterns	Requires tuning, over fitting
CNN	Imaging, handwriting	Automatic feature extraction	High data/computational needs
LSTM/RNN	Time series (gait, voice)	Sequence modeling	Complex training, memory

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

5. FEATURE EXTRACTION AND THEIR RELEVANCE IN PD DETECTION

The process of feature extraction is one of the most important in machine learning. Feature extraction defines the quality and relevance of information upon which a model will be trained. It differentiates between patients with Parkinsonism and healthy ones. The data modality provides a set of features that reflect various aspects of the disease. These aspects may be motor, cognitive, or physiological manifestations of the disease. This part discusses the nature of features that are frequently extracted out of different data sources and their diagnostic strength.

5.1 Voice and Speech Features

Early PD symptoms consist of changes in speech and phonation such as monotone speech and articulation problems, and hypophonia. These are measured based on acoustic characteristics derived out of the sustained phonation recordings or speech recording.

Common Features:

- **Jitter:** Jitter means frequency variation between cycles
- **Shimmer:** Amplitude variation is a measure that determines the difference in amplitude between two waveforms at the intersection point where the waveforms are coincident.
- **Fundamental frequency (F0)** and **harmonics to noise ratio (HNR)**
- **Mel Frequency Cepstral Coefficients (MFCCs):** Represent the spectral envelope of audio
- **Recurrence Period Density Entropy (RPDE)** and **Detrended Fluctuation Analysis (DFA)**

These features are frequently used with classifiers like SVM and RF, achieving high diagnostic accuracy [34].

5.2 Gait and Movement Features

Smartphone IMUs and wearable sensors record PD associated movement impairments, e.g. bradykinesia, postural instability, and tremors.

Extracted Features:

- Stride length and stride variability
- Step duration, step time asymmetry
- Tremor frequency components (typically 4–6 Hz)
- Acceleration entropy
- Root Mean Square (RMS) of acceleration
- Spectral power density of movement signals

These frequency domain and temporal characteristics are used in the detection of movement dysfunctions that are characteristic of PD [30].

5.3 Handwriting and Drawing Features

Micrographia and fine motor control impairments in PD are commonly assessed using digitized handwriting tasks, such as sentence writing or spiral drawing.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

Relevant Features:

- Pen pressure, stroke speed and pen lift time
- Writing duration and pauses
- Angle changes and curvature smoothness
- Dynamic Time Warping (DTW) similarity to reference spirals
- Kurtosis and skewness of velocity and acceleration

CNNs and LSTMs have demonstrated good performance in learning using these features, and frequently are more successful than handcrafted feature models [26].

5.4 Neuroimaging Features

Brain imaging provides both anatomical and functional information on the pathology of PD. Such pre-processing as spatial normalization and techniques of feature selection (e.g., PCA, ICA) must come before classification.

Commonly Used Features:

- Substantia nigra and basal ganglia volume of gray matter.
- FMRI functional connectivity matrices.
- Voxel based morphometry (VBM) features
- Intensity histograms and texture features
- DaTscan uptake ratios

These features are particularly suited for deep learning models and SVMs for early diagnosis of PD [19].

5.5 Biomarkers and Clinical Features

Early diagnostic possibilities are provided by biochemical and genetic data in combination with behavioural characteristics.

Extracted Features:

- Alpha synuclein, tau protein, amyloid beta CSF
- LRRK2, GBA, SNCA mutations
- Unified Parkinson's Disease Rating Scale (UPDRS) scores
- Olfactory function and REM sleep disorder data

These features are usually invasive or costly to run and restrict their standalone use [28].

Table 5: Summary of Features Extracted from Various Data Modalities

Data Type	Key Features	Diagnostic Relevance
Voice	Jitter, Shimmer, MFCC, RPDE, DFA	Early signs; high correlation with motor decline
Gait	Stride variability, step time, tremor frequency	Discriminates PD vs. controls in free living
Handwriting	Pressure, speed, curvature, pen lift time	Captures micrographia and motor coordination
Neuroimaging	Gray matter volume, connectivity, texture, intensity patterns	Reveals structural/functional degeneration
Biomarkers	CSF proteins, gene mutations, UPDRS	Biological basis of disease; supports diagnosis

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

6. MACHINE LEARNING IN THE DETECTION OF PARKINSON DISEASE: PERFORMANCE COMPARISON OF THE ALGORITHMS

The evaluation of performance is a vital aspect of any diagnostic system that uses the ML. In the case of Parkinson disease accuracy, sensitivity (true positive rate), and specificity (true negative rate) are some of the most common evaluation measures in the early diagnosis of the disease. This part of the paper will compare the performance of other ML algorithms in different research works, data types, and experimental conditions.

6.1 Evaluation Metrics Defined

- **Accuracy**: Accuracy measures the proportion of total correct predictions (both positive and negative) that are correctly identified by the model.

$$\text{Accuracy} = \frac{\text{TP+TN}}{\text{TP+TN+FP+FN}}$$

- **Sensitivity (Recall)**: Sensitivity measures the proportion of actual positive cases that are correctly identified by the model.

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP+FN}}$$

- **Specificity**: It measures the proportion of actual negatives correctly identified by the model.

$$\text{Specificity} = \frac{\text{TN}}{\text{TN+FP}}$$

- TP (True Positive): Correctly predicted positive
- TN (True Negative): Correctly predicted negative
- FP (False Positive): Incorrectly predicted positive (Type I Error)
- FN (False Negative): Incorrectly predicted negative (Type II Error)

These metrics must be balanced. High accuracy with low sensitivity may result in missed diagnoses of early stage PD.

6.2 Comparative Performance Overview

The following table summarizes performance reported in selected studies using benchmark datasets across common ML algorithms:

Table 6: Performance Comparison of ML Algorithms in Early PD Detection

Study	Data Type	ML Algorithm	Accuracy (%)	Sensitivity (%)	Specificity (%)
Tsanas et al. (2010) [22]	Voice (UCI)	SVM	91.4	89.5	92.3
Little et al. (2009) [31]	Voice	ANN	87.0	84.2	89.1
Trabassi, Dante et.al. (2019) [30]	Gait (mPower)	LSTM	93.7	92.0	94.5
Pereira et al. (2021) [26]	Drawing	CNN	94.0	93.5	94.2
R. Prashanth et al. (2018) [43]	Imaging + CSF	Random Forest	88.9	91.7	85.5
Sakar et al. (2019) [44]	Multimodal	Ensemble (SVM+RF)	95.4	96.0	94.2
Rehman et al., 2019 [182]	GAITRite; 303 participants (119 PD, 184 HC)	Random Forest (with information gain & RFE), SVM, logistic regression	97.14	100%	94%

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

6.3 Observations

- SVMs perform well with structured data like speech features and neuroimaging derived metrics.
- Deep learning models (CNNs, LSTMs) are superior in terms of raw or slightly processed data, gait time series and spiral drawings.
- Ensemble techniques are able to provide the optimal balanced performance in terms of metrics by using the capabilities of the individual classifiers.
- Sensitivity is particularly important for early detection to minimize false negatives.

6.4 Challenges in Performance Interpretation

Although numerical performance is commonly presented in an optimistic way in the literature, there are multiple factors influencing the generalizability:

- **Dataset biases**: Many studies rely on limited sample sizes or class imbalanced data.
- **Lack of external validation**: Most models are evaluated only via internal cross validation.
- **Feature over fitting**: This occurs with high dimensional inputs (e.g., neuroimaging).
- **Reproducibility issues**: Lack of code and dataset availability prevents reproducibility.

To mitigate these, recent studies emphasize the need for cross dataset validation, external test cohorts, and model interpretability benchmarks.

7. ENSEMBLE METHODS AND HYBRID APPROACHES IN PARKINSON'S DISEASE DETECTION

Individual machine learning (ML) models can achieve high accuracy in specific settings; they often suffer from limitations such as over fitting, sensitivity to feature noise, or poor generalization. To address these issues, ensemble methods which combine multiple models and hybrid approaches which integrate multiple data types have gained prominence in PD detection. These methods offer improved robustness, predictive power, and clinical relevance.

7.1 Ensemble Learning Techniques

Ensemble learning is another technique that improves predictive accuracy by combining the prediction of two or more base models. The important ensemble methods are:

- **Bagging (Bootstrap Aggregating):** This technique increases the stability of the model and decreases variance because it trains a variety of instances of a learning algorithm on various bootstrap samples (randomly resampled subsets) of the data and combines their predictions.

  Example: Random Forest is a classic bagging algorithm widely used in PD detection [45].
- **Boosting:** Sequentially builds models by focusing on instances the previous model misclassified.

  Example: AdaBoost and Gradient Boosting Machines (GBM) have shown improved sensitivity in voice based PD diagnosis [46].
- **Stacking:** Combines the predictions of multiple base learners using a meta model, often achieving better generalization than any single model.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

Example: A study by Sakar et al. employed a stacked ensemble of SVM, k-NN, and Decision Trees, improving classification performance on multimodal data [47].

7.2 Hybrid Approaches: Combining Data Modalities

Given Parkinson's disease's heterogeneous influence on motor, cognitive, and biological functions, multimodal data integration enhances the reliability of diagnostic models.

Examples of Hybrid Input Types:

- **Voice + Movement:** Combining speech features and gait metrics for improved detection in remote settings.
- **Neuroimaging + Clinical Scores:** Using MRI features along with UPDRS or MoCA scores for better phenotyping.
- **Sensor Data + Biomarkers:** Integrating wearable sensor readings with blood/CSF biomarkers or genetic markers.

Study Highlight: Prashanth et al. [48] developed a hybrid model using CSF biomarkers and SPECT imaging features, achieving 96% accuracy in early stage PD classification using a Random Forest classifier combined with rule based decision support.

7.3 Deep Ensemble and Multi Stream Architectures

Recent advancements in deep learning allow for more sophisticated ensemble and hybrid designs:

- **Deep Ensemble Networks:** Independently trained CNN or LSTM networks aggregated via voting or averaging for robust performance across modalities.
- **Multi Stream Neural Networks:** Architectures that process different data types (e.g., audio, motion, imaging) through parallel sub networks and fuse features at the decision layer.

Example: A multi stream CNN by Pereira et al. integrated spiral drawing and key stroke dynamics to classify PD patients with 95.6% accuracy [49].

7.4 Benefits of Ensemble and Hybrid Systems

Advantages	Implications for PD Detection
Reduced variance and bias	Better generalization across patient cohorts
Enhanced robustness to noise	Useful for wearable and at home monitoring scenarios
Integration of heterogeneous data	Captures multifaceted symptoms of PD
Modular and scalable architecture	Flexible deployment across clinical and telemedicine systems

7.5 Limitations and Considerations

- **Complexity:** Increased model size and interpretability issues.
- **Computational Cost:** Real time applications require optimization.
- **Data Synchronization:** Aligning multimodal data is non-trivial.
- **Need for Large, Diverse Datasets:** Over fitting remains a concern in small cohorts.

Despite these limitations, ensemble and hybrid approaches show strong promise for clinical deployment, particularly when combined with explainable AI and domain specific constraints.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

8. POTENTIAL OF WEARABLE DEVICES AND SMARTPHONES IN REAL TIME DATA COLLECTION FOR PD DETECTION

The current advances in the wearable device and smartphone sector to have sophisticated sensors have created an opportunity that can change the future of real time, continuous monitoring of Parkinson disease symptoms. These technologies are capable of recording rich ecologically valid data in non-clinical environments that allow an earlier diagnosis and improved disease management.

8.1 Types of Sensors and Data Collected

- **Accelerometers and Gyroscopes:** Measure movement dynamics including tremor amplitude, gait speed, and postural stability [50].
- **Microphones:** Capture voice and speech patterns affected by PD, enabling remote phonation analysis [34].
- **Touchscreens and Keyboard**s**:** Track fine motor skills through typing rhythm and pressure changes [49].
- **Heart Rate Monitors and Electrodermal Activity Sensors:** Offer insights into autonomic dysfunction related to PD [53].

8.2 Advantages of Real Time Monitoring

- **Continuous Symptom Tracking:** Allows detection of subtle motor fluctuations and medication effects that may not be captured during clinic visits.
- **Objective Quantification:** Provides quantitative data reducing subjective bias inherent in clinical rating scales like UPDRS.
- **Remote Assessment and Telemedicine:** Facilitates decentralized patient monitoring, reducing healthcare costs and improving access [54].
- **Data Richness:** Multimodal sensor data can be integrated to improve predictive accuracy of ML models.

8.3 Notable Wearable and Smartphone Based Studies

- **mPower Study:** A large scale mobile health initiative collecting gait, voice, and tapping data via iPhone sensors, enabling ML models to predict PD presence and symptom severity [55].
- **Parkinson@Home:** A system combining wrist worn sensors and smartphone apps to monitor tremor and bradykinesia in daily life [56].
- **Smartphone Voice Analysis:** Algorithms analyzing sustained phonation recorded by phones have achieved high sensitivity for early PD detection [31].

8.4 Challenges and Considerations

- **Data Quality and Noise:** Variability in sensor placement, environmental noise, and user compliance affect data reliability.
- **Privacy and Security:** Sensitive health data require stringent protections and user consent.
- **Battery Life and Usabilit**y**:** Devices must balance data sampling frequency with battery consumption to ensure continuous monitoring.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

- **Standardization and Validation:** Lack of standardized protocols complicates cross study comparisons and regulatory approval [58].

8.5 Future Directions

- **Integration with Cloud and Edge Computing:** Enabling real time processing and feedback while preserving user privacy.
- **Personalized Models:** Adapting algorithms to individual baselines to improve detection accuracy.
- **Multimodal Fusion:** Combining wearable sensor data with clinical and biomarker information for holistic assessment.

9. CHALLENGES AND LIMITATIONS OF CURRENT MACHINE LEARNING APPROACHES IN PARKINSON'S DISEASE DETECTION

Despite promising advances in ML for early detection of PD, several critical challenges and limitations hinder their clinical translation and widespread adoption. This section discusses key issues including data scarcity, quality concerns, and generalizability constraints.

9.1 Small Sample Sizes and Class Imbalance

- **Limited Dataset Availability:** Many PD datasets are small due to difficulties in recruiting early stage patients, leading to models trained on limited, potentially non representative samples [59].
- **Class Imbalance:** Healthy control subjects often outnumber PD patients, which can bias classifiers toward majority classes and inflate accuracy metrics without improving clinical utility [60].
- **Over fitting Risks:** Small sample sizes increase the risk of overfitting which is a phenomenon where the model fits the noise or other tendencies in the data available in training but when applied to unknown patient data the model fails.

9.2 Data Quality and Heterogeneity

- **Noisy and Missing Data:** Sensor artifacts, environmental noise, and missing values degrade model training and evaluation [58].
- **Variability across Devices and Protocols:** Differences in sensor types, data collection protocols, and clinical assessments introduce heterogeneity that complicates model standardization [59].
- **Labelling Errors:** Diagnostic errors and inconsistencies in clinical labelling of PD stages reduce the reliability of supervised learning approaches.

9.3 Generalizability across Populations and Settings

- **Demographic Biases:** Most datasets lack diversity in terms of age, ethnicity, and geography, limiting the applicability of models to wider populations [63].
- **Cross Dataset Transfer:** Models trained on one cohort often underperforms when applied to external datasets due to variations in data distribution [64].
- **Real World Variability:** Models validated under controlled clinical conditions may not perform equivalently in home or community settings.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

9.4 Algorithmic and Interpretability Challenges

- **Black Box Models:** Complex models such as deep neural networks provide limited interpretability, challenging clinical acceptance [65].
- **Feature Selection and Relevance:** Identifying robust, clinically meaningful features remains difficult given the multifactorial nature of PD [59].
- **Computational Complexity:** Resource intensive algorithms may be impractical for real time or edge device deployment.

9.5 Ethical and Regulatory Considerations

- **Privacy and Data Security:** Sensitive patient data should be handled in accordance with the regulations of General Data Protection Regulation (GDPR) and Health Insurance Portability and Accountability Act (HIPAA) [67].
- **Bias and Fairness:** Biases in the training data can lead to unequal or unfair predictions of diagnosis among various groups of patients. [68].
- **Clinical Validation and Approval:** Lack of standardized validation frameworks delays regulatory approval and clinical integration.

9.6 Strategies to Mitigate Challenges

- **Data Augmentation and Synthesis:** Techniques like SMOTE and GANs can alleviate sample size limitations [69].
- **Cross Validation and External Testing:** Rigorous evaluation protocols improve model robustness [70].
- **Explainable AI (XAI):** Incorporating interpretable models and post hoc explanations fosters clinical trust [71].
- **Collaborative Data Sharing:** Multi center consortia enable the aggregation of diverse, larger datasets [72].

10. ETHICAL CONSIDERATIONS AND POTENTIAL BIASES IN ML FOR PD DETECTION

The integration of ML in PD detection offers significant promise. But it also raises critical ethical issues and concerns about algorithmic bias that must be addressed to ensure equitable and trustworthy clinical applications.

10.1 Ethical Considerations

- **Privacy and Confidentiality:** ML models needs access to substantial amount of health data including genetic, clinical, and behavioural information. Ensuring robust data anonymization, encryption, and secure storage is vital to protect patient confidentiality [73].
- **Informed Consent:** Patients must be clearly informed about the intended use of their data, including secondary uses for model training and validation, with clear options for opting out [74].
- **Transparency and Explainability:** Clinicians and patients should understand how ML models make decisions to build trust and enable informed clinical judgments. Black box models challenge transparency, necessitating explainable AI (XAI) methods [75].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

- **Accountability and Liability:** Clear responsibility must be established for diagnostic errors or adverse outcomes related to ML tools. Accountability and liability of developers, clinicians, or healthcare institutions may involve who use ML tools [76].
- **Equitable Access:** Ensuring ML based diagnostics are accessible to diverse populations, including those in low resource settings, is essential to avoid exacerbating health disparities [77].

10.2 Potential Biases in Machine Learning Models

- **Data Bias:** Training datasets may underrepresent certain demographic groups (e.g., age, gender, ethnicity), leading to biased predictions and reduced accuracy for these populations [68].
- **Sampling Bias:** Sampling bias is evident in clinical cohorts, which frequently comprise patients exhibiting well-characterized symptoms, thereby overlooking typical or early-stage cases. This bias adversely impacts the generalizability of models. [79].
- **Measurement Bias:** Variability in data collection tools and protocols can introduce systematic errors influencing model outcomes [80].
- **Algorithmic Bias:** Model design choices, such as feature selection or loss functions, may inadvertently reinforce existing disparities [81].
- **Feedback Loops:** Deployment of biased models can perpetuate biases in clinical practice, affecting future data and decision making [82].

10.3 Strategies to Mitigate Ethical Concerns and Bias

- **Diverse and Representative Datasets:** Proactively including heterogeneous populations during data collection improves fairness [83].
- **Bias Detection and Auditing:** Regular evaluation of models for disparate performance across subgroups enables identification and correction of biases [84].
- **Explainable AI Techniques:** Methods such as SHAP, LIME, and counterfactual explanations enhance transparency [85].
- **Regulatory Frameworks:** Adherence to guidelines from bodies like the FDA and EMA for AI/ML in healthcare ensures safety and ethical compliance [86].
- **Stakeholder Engagement:** Involving patients, clinicians, ethicists, and data scientists collaboratively promotes balanced perspectives in model development [87].

11. INTEGRATION OF MACHINE LEARNING MODELS INTO CLINICAL PRACTICE AND IMPACT ON PATIENT CARE

The translation of machine learning (ML) models from research settings into clinical practice for Parkinson's disease (PD) detection holds transformative potential to enhance diagnosis, personalize treatment, and improve patient outcomes. However, successful integration requires overcoming multiple technical, operational, and ethical hurdles.

11.1 Clinical Workflow Integration

- **Seamless Embedding:** ML tools must be integrated into existing clinical workflows, electronic health records (EHRs), and diagnostic platforms to avoid disruption and facilitate clinician adoption [88].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

- **User Friendly Interfaces:** Interfaces providing clear, actionable insights rather than raw predictions enable clinicians to interpret and trust ML outputs [89].
- **Decision Support Systems (DSS):** ML models can functions decision support tools, assisting neurologists for early PD diagnosis, differential diagnosis, and monitoring disease progression [90].

11.2 Enhancing Diagnostic Accuracy and Speed

- **Early and Objective Diagnosis:** ML based tools can detect subtle patterns in clinical, imaging, or sensor data, enabling earlier diagnosis than traditional clinical assessment alone [91].
- **Reduction of Diagnostic Errors:** Automated systems have the potential to minimize human mistakes and reduce variability among different evaluators in diagnosing PD [92].
- **Continuous Monitoring:** Wearable and smartphone based ML systems allow real time symptom tracking and can alert clinicians to disease progression or treatment response [93].

11.3 Personalized Treatment and Prognosis

- **Stratification of Patients:** ML can identify PD subtypes and progression trajectories, aiding tailored therapeutic strategies [94].
- **Treatment Optimization:** Predictive models can forecast treatment response, side effects, and guide medication adjustments [95].
- **Remote Patient Management:** Telemedicine platforms integrated with ML enable remote monitoring and timely interventions. This improves access to care especially in underserved areas [96].

11.4 Challenges to Clinical Adoption

- **Validation and Regulatory Approval:** Rigorous clinical trials and compliance with regulatory standards (e.g., FDA, EMA) are necessary for ML tools to be trusted and approved [97].
- **Interpretability and Trust:** Clinicians require explainable models to understand and rely on AI driven recommendations [98].
- **Data Privacy and Security:** Ensuring patient data confidentiality within clinical systems is paramount [67].
- **Training and Education:** Clinicians must be adequately trained to understand ML capabilities and limitations to effective use of these tools [100].

11.5 Potential Impact on Patient Care

- **Improved Patient Outcomes:** Earlier diagnosis and personalized care can slow disease progression and enhance quality of life [101].
- **Healthcare Efficiency:** Automation of diagnostic processes can reduce clinician workload and healthcare costs [100].
- **Empowered Patients:** Real time feedback and monitoring enable patients to participate actively in their care [103].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

12. EMERGING TRENDS

As ML continues to evolve, several emerging trends show promise in addressing existing challenges in PD detection, particularly enhancing interpretability, privacy, and model robustness.

12.1 Explainable AI (XAI)

- **Need for Transparency:** Conventional ML and deep learning models function as black boxes, which can hinder clinical trust and real-world adoption. XAI techniques seek to enhance model decisions, making outputs interpretable and clinically actionable [104].
- **Techniques:** Methods such as LIME (Local Interpretable Model agnostic Explanations), SHAP (SHapley Additive exPlanations) and attention mechanisms facilitate understanding of feature contributions and the reasoning underlying model outputs. [85].
- **Clinical Impact:** XAI fosters trust by enabling clinicians to validate model predictions against medical knowledge, detect biases, and improve decision making confidence [106].
- **Current Research:** Studies applying XAI to PD detection models have demonstrated improved understanding of symptom relevance and biomarker contributions [107].

12.2 Federated Learning

- **Privacy Preserving Collaboration:** Federated learning enables decentralized training of ML models across multiple institutions without sharing sensitive patient data, thereby preserving privacy and complying with data protection regulations [108].
- **Addressing Data Scarcity:** By aggregating learning from distributed datasets, federated learning improves model generalizability and performance, overcoming the challenge of small, localized datasets [109].
- **Applications in PD:** Early implementations show federated models leveraging multi center clinical, imaging, and sensor data to enhance early PD detection accuracy [73].
- **Technical Challenges:** Issues such as communication overhead, data heterogeneity, and model convergence require further research [111].

12.3 Integration with Multimodal and Longitudinal Data

- Leveraging multimodal data fusion (combining neuroimaging, genomics, speech, and wearable sensor data) and longitudinal data analytics provides a more comprehensive understanding of PD progression [112]. Advanced ML architectures such as transformers and graph neural networks are being explored for this purpose [113].

12.4 Edge Computing and Real Time Analysis

- Deploying ML models on edge devices like smartphones and wearables allows real time, low latency PD symptom monitoring and alerts, enhancing patient engagement and timely clinical intervention [114].

12.5 Synthetic Data Generation

- Techniques like generative adversarial networks (GANs) are used to generate synthetic health data to augment training datasets, addressing data scarcity and balancing demographic representation [115].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

13. COMBINING MACHINE LEARNING WITH GENOMICS, PROTEOMICS, AND OTHER TECHNOLOGIES FOR COMPREHENSIVE EARLY DETECTION

The integration of ML with high throughput omics technologies such as genomics and proteomics offers promising avenues for advancing early detection and understanding of PD beyond traditional clinical and sensor based data.

13.1 Genomics and ML

- **Genetic Risk Profiling:** Genome wide association studies (GWAS) have uncovered multiple genetic variants that are associated with an increased susceptibility to PD. ML models can analyze complex interactions among these variants to predict individual susceptibility and onset risk [116].
- **Polygenic Risk Scores:** ML algorithms help compute polygenic risk scores that aggregate multiple genetic factors, improving prediction accuracy over single marker approaches [117].
- **Personalized Medicine:** Understanding genetic subtypes through ML can guide tailored prevention and therapeutic interventions [118].

13.2 Proteomics and Biomarker Discovery

- **Protein Expression Patterns:** Proteomic profiling detects alterations in protein abundance and post translational modifications associated with early PD pathology [119].
- **ML based Biomarker Selection:** Feature selection methods in ML identify key protein biomarkers from high dimensional proteomic datasets, enhancing diagnostic models [120].
- **Non Invasive Diagnostics:** Proteomic signatures in bio fluids such as cerebrospinal fluid (CSF) and blood hold potential for minimally invasive early detection [121].

13.3 Multi Omics Data Integration

- **Holistic Disease Characterization:** Combining genomics, proteomics, metabolomics, and transcriptomics data provides a comprehensive view of PD pathophysiology [122].
- **Advanced ML Models:** Techniques like multi view learning and deep learning architectures integrate heterogeneous omics datasets to improve early diagnosis and patient stratification [123].
- **Challenges:** Data heterogeneity, batch effects, and computational complexity necessitate robust pre-processing and model design [124].

13.4 Other Emerging Technologies

- **Epigenetics:** ML models analyzing DNA methylation and histone modification data reveal additional layers of PD risk and progression markers [125].
- **Microbiome:** Gut microbiota profiles linked to PD are emerging as novel data sources for ML based predictive models [126].
- **Neuroinflammation and Metabolomics:** Integration of inflammatory markers and metabolic profiles further enrich predictive capabilities [127].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

13.5 Clinical Implications

- The convergence of ML with multi omics and novel biomarkers can enable earlier, more accurate PD diagnosis, better prognosis, and individualized therapeutic strategies, thereby moving towards precision neurology [128].

14. THE NEED FOR LARGE SCALE, MULTI CENTER STUDIES TO VALIDATE MACHINE LEARNING MODELS FOR PARKINSON'S DETECTION

14.1 Importance of Large Scale Validation

- **Robustness and Generalizability:** ML models developed for PD detection often suffer from overfitting to small or homogeneous datasets, limiting their applicability to diverse patient populations [91]. Large scale studies encompassing heterogeneous cohorts are essential to ensure robustness and generalizability across demographics, disease stages, and comorbidities [130].
- **Reproducibility:** Validation across multiple independent centers addresses issues related to reproducibility, a critical factor for clinical adoption of ML based diagnostic tools [131].

14.2 Multi Center Collaboration Advantages

- **Diverse Data Acquisition:** Multi center studies enable pooling of diverse data modalities such as genomics, neuroimaging, wearable sensor data and clinical assessments enriching training datasets for ML models [132].
- **Standardization of Protocols:** Collaborative efforts facilitate the establishment of standardized data collection, labelling, and pre-processing protocols, which are vital for reducing batch effects and biases [133].
- **Resource Sharing:** Access to larger datasets and computational resources accelerates model development and benchmarking [134].

14.3 Challenges in Multi Center Studies

- **Data Privacy and Governance:** Sharing sensitive patient data across centers raises ethical and legal challenges; solutions such as federated learning (discussed in Section 12) can help mitigate these concerns [135].
- **Data Heterogeneity:** Variations in data acquisition devices, protocols, and population characteristics introduce heterogeneity that ML models must be robust against [136].
- **Coordination and Funding:** Organizing large scale multi center studies requires significant coordination, funding, and long term commitment from participating institutions [137].

14.4 Successful Examples and Future Directions

- Notable initiatives such as the Parkinson's Progression Markers Initiative (PPMI) and the Oxford Parkinson's Disease Centre (OPDC) have demonstrated the value of large, multi center datasets in advancing PD research and ML model development [138].
- Future efforts should prioritize open data sharing, interoperability, and integration of multi-omics and real world data to further improve early detection and personalized care [139].

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

15. CONCLUSION AND FUTURE DIRECTIONS

The use of ML in the initial diagnosis of PD has a great potential to transform diagnosis, prognosis, and individualized treatment. Although a significant progress has been assessed in this paper, there are still a few opportunities that can be explored and developed further to discover the full potential of ML in clinical practice.

15.1 Summary of Key Insights

- ML methods have been shown to be able to perform well with different forms of data, such as neuroimaging, voice, movement, and biomarkers [91].
- Incorporation of new technologies, including genomics, proteomics and wearable sensors, enhances the quality of data and predictive ability [141].
- Large scale validation studies that are multi centre are essential in order to guarantee model generalizability and clinical reliability [142].
- Ethical considerations, interpretable models, and data privacy should be well taken care of to enable adoption [143].

15.2 Future Research Directions

- **Explainable AI (XAI):** It will be necessary to build explicit and explainable ML models that will increase trust in clinicians and enhance decision making [144].
- **Federated and Privacy Preserving Learning:** Enhancing methods for decentralized learning will address data sharing constraints while leveraging larger datasets [145].
- **Multi Modal and Multi Omics Integration:** Continued research on harmonizing heterogeneous data sources will provide deeper insights into PD pathophysiology and early markers [146].
- **Real World Data and Digital Biomarkers:** Utilizing longitudinal, real time data from smartphones and wearables can improve continuous monitoring and early intervention [147].
- **Personalized Prediction Models:** Tailoring ML models to individual genetic and environmental profiles may enhance accuracy and therapeutic outcomes [148].
- **Automated Data Annotation and Quality Control:** Advances in unsupervised learning and data augmentation will help overcome data scarcity and labelling challenges [149].
- **Cross Disease Applications:** Transfer learning from related neurodegenerative diseases may improve detection sensitivity and broaden applicability [70].

15.3 Conclusion

The convergence of machine learning with advances in biomedical data acquisition, computing power, and interdisciplinary collaboration is rapidly changing the landscape of Parkinson's disease diagnosis. By addressing current challenges and fostering innovation, future research will enable earlier, more accurate and patient cantered detection methods, ultimately improving quality of life and clinical outcomes for those affected by PD.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

16. DECLARATION

16.1 Use of AI Technology

The authors used AI-based tools for language refinement and editing purposes only. All content was reviewed, verified, and approved by the authors, who take full responsibility for the final manuscript.

16.2 Conflicts of Interest Declaration

All authors declare that they have no conflicts of interest.

16.3 Informed Consent Declaration

No, my research did not involve human participants.

References

1) J. Parkinson, "An Essay on the Shaking Palsy," Sherwood, Neely, and Jones, London, 1817.
2) M. Fearnley and A. Lees, "Ageing and Parkinson's disease: substantia nigra regional selectivity," *Brain*, vol. 114, no. 5, pp. 2283–2301, 1991.
3) W. Poewe et al., "Parkinson disease," *Nature Reviews Disease Primers*, vol. 3, no. 1, pp. 1–21, 2017.
4) Olanow CW, Stern MB, Sethi K. "The scientific and clinical basis for the treatment of Parkinson disease," Neurology. 2009.
5) Postuma RB, Berg D, Stern M, et al. "MDS clinical diagnostic criteria for Parkinson's disease," Movement Disorders. 2015.
6) A. Das et al., "Predicting Parkinson's disease using machine learning: A review," *Journal of Biomedical Informatics*, vol. 84, pp. 100–110, 2018.
7) A. Prashanth and S. Roy, "Early detection of Parkinson's disease through patient questionnaire and predictive modelling," *Expert Systems with Applications*, vol. 66, pp. 111–119, 2016.
8) J. Jankovic, "Parkinson's disease: clinical features and diagnosis," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 79, no. 4, pp. 368–376, 2008.
9) D. Hughes et al., "Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico pathological study of 100 cases," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 55, no. 3, pp. 181–184, 1992.
10) Daniela Berg, "Biomarkers for the Early Detection of Parkinson's and Alzheimer's Disease," *Neurodegener Dis (2008) 5 (3-4): 133–136.*
11) D. Sakar et al., "A comparative analysis of speech signal processing algorithms for Parkinson's disease classification and the use of the tunable Q factor wavelet transform," *Applied Soft Computing*, vol. 74, pp. 255–263, 2019.
12) Suyao Wei et al., "The Application of Wearable Sensors and Machine Learning Algorithms in Rehabilitation Training: A Systematic Review" *Sensors (Basel) 2023 Sep 5; 23 (18):7667*.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

13) A. Arora et al., "High accuracy discrimination of Parkinson's disease participants from healthy controls using smartphones," *Journal of Parkinson's Disease*, vol. 5, no. 4, pp. 869–873, 2015.

14) Jintao Yu et al., "Improved Deep Learning for Parkinson's Diagnosis Based on Wearable Sensors". *Electronics 2024, 13, 4638. https://doi.org/ 10.3390/electronics13234638*.

15) Zeighami, Yashar et al. "A clinical-anatomical signature of Parkinson's disease identified with partial least squares and magnetic resonance imaging." NeuroImage vol. 190 (2019): 69-78. doi:10.1016/j.neuroimage.2017.12.050.

16) Scherfler C., et al. "Diagnostic potential of neuroimaging in early Parkinson's disease." Movement Disorders, 2007;22(10):1478–1485

17) M. Little et al., "Exploiting non- linear recurrence and fractal scaling properties for voice disorder detection," *Biomedical Engineering Online*, vol. 6, no. 23, 2007.

18) A. Tsanas et al., "Accurate telemonitoring of Parkinson's disease progression by non invasive speech tests," *IEEE Transactions on Biomedical Engineering*, vol. 57, no. 4, pp. 884–893, 2010.

19) Yodpijit et al., "The use of smartphone for gait analysis". 543-546. 10.1109/ICCAR.2017.7942756.

20) Rovini E., Maremmani C., Cavallo F. "How wearable sensors can support Parkinson's disease diagnosis and treatment: A systematic review". Sensors, 2017;17(6):1304.

21) Kamila Białek et al., " Analysis of Handwriting for Recognition of Parkinson's Disease: Current State and New Study," *Electronics 2024, 13(19), 3962*.

22) R. Pereira et al., "Deep learning with CNNs for Parkinson's disease assessment using spiral drawing tests," *Sensors*, vol. 21, no. 4, p. 1211, 2021.

23) C. Klein and A. Westenberger, "Genetics of Parkinson's disease," *Cold Spring Harbor Perspectives in Medicine*, vol. 2, no. 1, 2012.

24) B. Mollenhauer et al., "Combined biomarkers in Parkinson's disease: A roadmap for development and discovery," *Movement Disorders*, vol. 35, no. 5, pp. 716–733, 2020.

25) Li Y., et al. "Deep learning based imaging data classification for Parkinson's disease". Biomedical Signal Processing and Control, 2019;47:428–435.

26) D. Trabassi et al., "Machine Learning Approach to Support the Detection of Parkinson's Disease in IMU Based Gait Analysis," Sensors, vol. 22, no. 10, Art. no. 3700, 2022.

27) M. Little et al., "Suitability of dysphonia measurements for telemonitoring of Parkinson's disease," *IEEE Transactions on Biomedical Engineering*, vol. 56, no. 4, pp. 1015–1022, 2009.

28) Sarkar M., et al. "Deep learning for Parkinson's disease classification: A deep autoencoder-based approach". Computer Methods and Programs in Biomedicine, 2020;184:105268

29) A. Tsanas et al., "Novel speech signal processing algorithms for high accuracy classification of Parkinson's disease," *IEEE Transactions on Biomedical Engineering*, vol. 59, no. 5, pp. 1264–1271, 2012.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

30) Zhang Y., et al. “Voxel-based morphometry and machine learning for early Parkinson’s disease diagnosis”.NeuroImage: Clinical, 2015;7:406–412.

31) Oh J., et al. “Classification of Parkinson’s disease using convolutional neural networks with brain MRI,” Computer Methods and Programs in Biomedicine, vol. 179, pp. 105–113, 2019.

32) R. Prashanth et.al., “Early detection of Parkinson’s disease through patient questionnaire and biomarkers using machine learning,” *International Journal of Medical Informatics*, Volume 119,Pages 75-87, 2018.

33) B. E. Sakar et al., “Collection and analysis of a Parkinson speech dataset with multiple types of sound recordings,” *IEEE Journal of Biomedical and Health Informatics, vol. 17, no. 4, pp. 828-834, July 2013*.

34) L. Breiman, “Random forests,” *Machine Learning*, vol. 45, no. 1, pp. 5–32, 2001.

35) Nishat, Mirza Muntasir et al. “Detection of Parkinson's Disease by Employing Boosting Algorithms.” 2021 Joint 10th International Conference on Informatics, Electronics & Vision (ICIEV) and 2021 5th International Conference on Imaging, Vision & Pattern Recognition (icIVPR) (2021): 1-7.

36) H. O. Sakar, et.al., “Machine learning methods for classification of Parkinson’s disease using voice data,” Applied Soft Computing, vol. 17, pp. 828–836, 2014..

37) R. Prashanth et al., “High-Accuracy Classification of Parkinson's Disease Through Shape Analysis and Surface Fitting in ^{123}I-Ioflupane SPECT Imaging,” *IEEE Journal of Biomedical and Health Informatics*, 2016.

38) C. R. Pereira, et.al., “Deep learning–aided Parkinson’s disease diagnosis from handwritten dynamics,” in Proc. 29th Conf. Graph., Patterns Images (SIBGRAPI), 2016, pp. 340–346.

39) Silvia Del Din et al., “Free-living gait characteristics in ageing and Parkinson’s disease: impact of environment and ambulatory bout length,” *Journal of NeuroEngineering and Rehabilitation*, vol. 15, no. 1, p. 73, 2016.

40) Masashi Suzuki et al., “Wearable sensor device-based detection of decreased heart rate variability in Parkinson's disease,” *J Neural Transm (Vienna). 2022 Oct;129(10):1299-1306*.

41) M. Espay et al., “Technology in Parkinson’s disease: Challenges and opportunities,” *Movement Disorders*, vol. 31, no. 9, pp. 1272–1282, 2016.

42) S. Bot et al., “The mPower study, Parkinson disease mobile data collected using ResearchKit,” *Scientific Data*, vol. 3, p. 160011, 2016.

43) Moreau, Caroline et al. “Overview on wearable sensors for the management of Parkinson's disease.” NPJ Parkinson's disease vol. 9,1 153. 2 Nov. 2023, doi:10.1038/s41531-023-00585-y

44) J. Godinho et al., “A systematic review of the characteristics and validity of monitoring technologies to assess Parkinson’s disease,” *Journal of NeuroEngineering and Rehabilitation*, vol. 13, no. 1, p. 24, 2016.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

45) Shokrpour, Sahar et.al. "Machine learning for Parkinson's disease: a comprehensive review of datasets, algorithms, and challenges." npj Parkinson's Disease. (2025).11. 10.1038/s41531-025-01025-9.

46) H. He and E. A. Garcia, "Learning from imbalanced data," *IEEE Transactions on Knowledge and Data Engineering*, vol. 21, no. 9, pp. 1263–1284, 2009.

47) Paul, Sudip et al. "Bias Investigation in Artificial Intelligence Systems for Early Detection of Parkinson's Disease: A Narrative Review." Diagnostics (Basel, Switzerland) vol. 12,1 166. 11 Jan. 2022, doi:10.3390/diagnostics12010166.

48) Hires, Mate et al. "On the inter-dataset generalization of machine learning approaches to Parkinson's disease detection from voice." International journal of medical informatics vol. 179 (2023): 105237. doi:10.1016/j.ijmedinf.2023.105237.

49) Holzinger, Andreas et al. "Causability and explainability of artificial intelligence in medicine." Wiley interdisciplinary reviews. Data mining and knowledge discovery vol. 9,4 (2019): e1312. doi:10.1002/widm.1312.

50) Yadav, Neel et al. "Data Privacy in Healthcare: In the Era of Artificial Intelligence." Indian dermatology online journal vol. 14,6 788-792. 27 Oct. 2023, doi:10.4103/idoj.idoj_543_23.

51) N. Mehrabi et al., "A survey on bias and fairness in machine learning," *ACM Computing Surveys*, vol. 54, no. 6, pp. 1–35, 2021.

52) N. Chawla et al., "SMOTE: Synthetic minority over sampling technique," *Journal of Artificial Intelligence Research*, vol. 16, pp. 321–357, 2002.

53) J. C. Vásquez-Correa et al., "Convolutional Neural Networks and a Transfer Learning Strategy to Classify Parkinson's Disease from Speech in Three Different Languages," *arXiv:2002.04374v1 [cs.LG]*.

54) F. Doshi Velez and B. Kim, "Towards a rigorous science of interpretable machine learning," *arXiv preprint arXiv:1702.08608*, 2017.

55) Hill DL,et.al., "Metadata Framework to Support Deployment of Digital Health Technologies in Clinical Trials in Parkinson's Disease". Sensors, 2022; 22(6):2136. https://doi.org/10.3390/s22062136.

56) Rieke, N., Hancox, J., Li, W. et al., "The future of digital health with federated learning." npj Digit. Med. 3, 119 (2020). https://doi.org/10.1038/s41746-020-00323-1.

57) Martinez-Martin, N., Insel, T.R., Dagum, P. et al., "Data mining for health: staking out the ethical territory of digital phenotyping." npj Digital Med 1, 68 (2018).

58) J. Amann, et.al., "Explainability for artificial intelligence in healthcare: a multidisciplinary perspective," BMC Medical Informatics and Decision Making, vol. 20, article 310, 2020.

59) Prachi Bagave, et al., "Accountability Framework for Healthcare AI Systems: Towards Joint Accountability in Decision Making," *https://arxiv.org/pdf/2509.03286*

60) W. H. Organization, "Ethics and governance of artificial intelligence for health," World Health Organization, Geneva, Switzerland, 2021

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

61) Cross, James L et al. "Bias in medical AI: Implications for clinical decision-making." PLOS digital health vol. 3, 11 e0000651. 7 Nov. 2024, doi:10.1371/journal.pdig.0000651.

62) Mittermaier, M., Raza, M.M. & Kvedar, J.C. "Bias in AI-based models for medical applications: challenges and mitigation strategies". npj Digit. Med. 6, 113 (2023).

63) D. Raji and A. Buolamwini, "Actionable auditing: Investigating the Impact of Publicly Naming Biased Performance Results of Commercial AI Products," *Proceedings of the AAAI/ACM Conference on AI Ethics*, pp. 429–435, 2019.

64) S. Barocas, M. Hardt, and A. Narayanan, "Fairness and Machine Learning: Limitations and Opportunities," MIT Press, 2023.

65) Ueda, Daiju et al. "Fairness of artificial intelligence in healthcare: review and recommendations." Japanese journal of radiology vol. 42, 1 (2024): 3-15. Doi: 10.1007/s11604-023-01474-3.

66) S. B. Ghassemi et al., "Bias Detection in Clinically Machine Learning Models," *IRE Journals.* Volume 9 Issue 3, SEP 2025.

67) M. T. Lundberg and S. Lee, "A unified approach to interpreting model predictions," *Advances in Neural Information Processing Systems*, vol. 30, pp. 4765–4774, 2017.

68) U.S. Food and Drug Administration (FDA), "Proposed regulatory framework for AI/ML based software as a medical device," 2019.

69) A. Vayena, et.al.,"Machine learning in medicine: Addressing ethical challenges," PLoS Medicine, vol. 15, no. 11, e1002689, 2018.

70) Kotter, Elmar, et.al., "Challenges and solutions for introducing artificial intelligence (AI) in daily clinical workflow." European radiology vol. 31,1 (2021): 5-7. doi:10.1007/s00330-020-07148-2.

71) Schreier, Meredith et al. "User-Centered Delivery of AI-Powered Health Care Technologies in Clinical Settings: Mixed Methods Case Study." JMIR human factors vol. 12 e76241. 26 Aug. 2025, doi:10.2196/76241.

72) Pedersen, Mangor et al. "Artificial intelligence for clinical decision support in neurology." Brain communications vol. 2,2 fcaa096. 9 Jul. 2020, doi:10.1093/braincomms/fcaa096.

73) Jie Mei, et al., "Machine Learning for the Diagnosis of Parkinson's Disease: A Review of Literature," *Frontiers in Aging Neuroscience*, vol. 13, 2021.

74) Taylor, R Andrew et al. "Leveraging artificial intelligence to reduce diagnostic errors in emergency medicine: Challenges, opportunities, and future directions." Academic emergency medicine : official journal of the Society for Academic Emergency Medicine vol. 32,3 (2025): 327-339. doi:10.1111/acem.15066.

75) Jha, Ashwani et al. "Digital Biomarkers in Parkinson's Disease: Missing the Forest for the Trees?." Movement disorders clinical practice vol. 10,Suppl 2 S68-S72. 17 May. 2023, doi:10.1002/mdc3.13746.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

76) Dadu, Anant et al. “Identification and prediction of Parkinson's disease subtypes and progression using machine learning in two cohorts.” NPJ Parkinson's disease vol. 8,1 172. 16 Dec. 2022, doi:10.1038/s41531-022-00439-z.

77) R. Ahmadi Rastegar, et.al., “Parkinson’s progression prediction using machine learning and serum cytokines,” npj Parkinson’s Disease, vol. 5, article 14, 2019.

78) van den Bergh, Robin et al. “The state of telemedicine for persons with Parkinson's disease.” Current opinion in neurology vol. 34,4 (2021): 589-597. doi:10.1097/WCO.0000000000000953

79) FDA, “Artificial intelligence and machine learning in software as a medical device,” 2021.

80) F. Doshi Velez and B. Kim, “Explainable AI for clinical decision making,” *arXiv preprint arXiv:1702.08608*, 2017.

81) Topol, Eric J. “High-performance medicine: the convergence of human and artificial intelligence.” Nature medicine vol. 25,1 (2019): 44-56. doi:10.1038/s41591-018-0300-7.

82) Bloem, Bastiaan R et al. “Integrated and patient-centred management of Parkinson's disease: a network model for reshaping chronic neurological care.” The Lancet. Neurology vol. 19,7 (2020): 623-634. doi:10.1016/S1474-4422(20)30064-8.

83) Sham, Sunder et al. “Empowering Patients Through Digital Health Literacy and Access to Electronic Medical Records (EMRs) in the Developing World.” Cureus vol. 16,4 e57527. 3 Apr. 2024, doi:10.7759/cureus.57527.

84) A. Tjoa and C. Guan, “A survey on explainable artificial intelligence (XAI): toward medical XAI,” *IEEE Transactions on Neural Networks and Learning Systems*, vol. 32, no. 11, pp. 4793–4813, 2021.

85) G. Holzinger et al., “Towards explainable AI in healthcare,” *Machine Learning and Knowledge Extraction*, vol. 1, no. 1, pp. 1–20, 2019.

86) Shen, Matthew et al. “Explainable artificial intelligence to diagnose early Parkinson's disease via voice analysis.” Scientific reports vol. 15,1 11687. 5 Apr. 2025, doi:10.1038/s41598-025-96575-6.

87) P. Kairouz et al., “Advances and open problems in federated learning,” *Foundations and Trends® in Machine Learning*, vol. 14, no. 1–2, pp. 1–210, 2021.

88) J. Sheller et al., “Federated learning in medical imaging,” *Artificial Intelligence in Medicine*, vol. 112, p. 102 47, 2021.

89) Tian Li et al., “Federated learning: challenges, methods, and future directions,” *IEEE Signal Processing Magazine*, vol. 37, no. 3, pp. 50–60, 2020.

90) F. A. Alsheikh et al., “Multimodal data fusion for Parkinson’s disease diagnosis,” *Sensors*, vol. 20, no. 4, p. 1119, 2020.

91) S. Naimi, et.al.,“1D-Convolutional transformer for Parkinson disease diagnosis from gait,” arXiv, 2023.

92) Khan, S., et al. “EIoT: edge of things for Parkinson’s disease prediction in healthcare.” Journal on Wireless Communication and Networking 2025, 97 (2025).

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

93) Maayan Frid-Adar, et.al.,"GAN-based synthetic medical image augmentation for increased CNN performance in liver lesion classification," Neurocomputing, vol. 321, pp. 321–331, 2018

94) Nalls, Mike A et al. "Large-scale meta-analysis of genome-wide association data identifies six new risk loci for Parkinson's disease." Nature genetics vol. 46,9 (2014): 989-93. doi:10.1038/ng.3043.

95) Sia, Ming-Wei et al. "Polygenic Risk Scores in a Prospective Parkinson's Disease Cohort." Movement disorders: official journal of the Movement Disorder Society vol. 36, 12 (2021): 2936-2940. doi:10.1002/mds.28761

96) F. Soldner and R. Jaenisch, "Stem cells, genome editing and the path to translational medicine," Cell, vol. 175, no. 3, pp615–632, 2018.

97) Licker, Virginie et al. "Proteomics in human Parkinson's disease research." Journal of proteomics vol. 73, 1 (2009): 10-29. doi:10.1016/j.jprot.2009.07.007.

98) Simon Lam et.al., "Machine learning Analysis Reveals Biomarkers for the detection for Neurological Diseases," *Frontiers in Neuroscience*, vol. 14, p. 651, 2020.

99) Andersen, A D et al. "Cerebrospinal fluid biomarkers for Parkinson's disease - a systematic review." Acta neurologica Scandinavica vol. 135,1 (2017): 34-56. doi:10.1111/ane.12590.

100) Wang, Wang et al. "Multi-Omics Integration in Mice with Parkinson's Disease and the Intervention Effect of Cyanidin-3-O-Glucoside." Frontiers in aging neuroscience vol. 14 877078. 29 Apr. 2022, doi:10.3389/fnagi.2022.877078

101) N. Rappoport and R. Shamir, "Multi-omic and multi-view clustering algorithms: review and cancer benchmark," Nucleic Acids Research, vol. 46, no. 20, pp. 10546–10562, 2018.

102) López de Maturana, Evangelina et al. "Challenges in the Integration of Omics and Non-Omics Data." Genes vol. 10,3 238. 20 Mar. 2019, doi:10.3390/genes10030238.

103) Pavlou, et.al.,"Epigenetics in Parkinson's Disease." Advances in experimental medicine and biology vol. 978 (2017): 363-390. doi:10.1007/978-3-319-53889-1_19.

104) Grace Hey et al αl., "Therapies for Parkinson's disease and the gut microbiome: evidence for bidirectional connection," *Frontiers in Aging Neuroscience*, 2023.

105) Y. Shao and W. Le,"Recent advances and perspectives of metabolomics-based investigations in Parkinson's disease," Molecular Neurodegeneration, vol. 14, article 3, 2019.

106) Espay, Alberto J et al. "Precision medicine for disease modification in Parkinson disease." Nature reviews. Neurology vol. 13,2 (2017): 119-126. doi:10.1038/nrneurol.2016.196.

107) Tabashum, Thasina et al. "Machine Learning Models for Parkinson Disease: Systematic Review." JMIR medical informatics vol. 12 e50117. 17 May. 2024, doi:10.2196/50117.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

108) McDermott, Matthew B A et al. "Reproducibility in machine learning for health research: Still a ways to go." Science translational medicine vol. 13,586 (2021): eabb1655. doi:10.1126/scitranslmed.abb1655.

109) Ofori, Edward et al. "Parkinson's disease biomarkers program brain imaging repository." NeuroImage vol. 124,Pt B (2016): 1120-1124. doi:10.1016/j.neuroimage.2015.05.005.

110) Bento, Mariana et al. "Deep Learning in Large and Multi-Site Structural Brain MR Imaging Datasets." Frontiers in neuroinformatics vol. 15 805669. 20 Jan. 2022, doi:10.3389/fninf.2021.805669

111) Danek, Benjamin et al. "Federated Learning for multi-omics: a performance evaluation in Parkinson's disease." bioRxiv: the preprint server for biology 2023.10.04.560604. 12 Feb. 2024, doi:10.1101/2023.10.04.560604. Preprint.

112) P. Kairouz et al., "Federated learning: Challenges and opportunities," *IEEE Signal Processing Magazine*, vol. 37, no. 3, pp. 50–60, 2020.

113) A. S. Chandrabhatla, et.al., "Co-evolution of machine learning and digital technologies to improve monitoring of Parkinson's disease motor symptoms," npj Digital Medicine, vol. 5, article 32, 2022.

114) Chung, Kevin C et al. "A guide to organizing a multicenter clinical trial." Plastic and reconstructive surgery vol. 126, 2 (2010): 515-523. doi:10.1097/PRS.0b013e3181df64fa.

115) Parkinson's Progression Markers Initiative (PPMI) Consortium, "The Parkinson Progression Markers Initiative (PPMI)," *Progress in Neurobiology*, vol. 95, no. 4, pp. 629–635, 2011.

116) Marek, Kenneth et al. "The Parkinson's progression markers initiative (PPMI) - establishing a PD biomarker cohort." Annals of clinical and translational neurology vol. 5, 12 1460-1477. 31 Oct. 2018, doi:10.1002/acn3.644.

117) T. Chen and Y. Guestrin, "XGBoost: A scalable tree boosting system," *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, 2016.

118) Ya Yang, et.al., "Deep learning in large and multi-site structural brain MRI datasets," Frontiers in Neuroinformatics, vol. 15, art. 805669, 2021.

119) J. Zhang and Z. M. Zhang, "Ethics and governance of trustworthy medical artificial intelligence," BMC Medical Informatics and Decision Making, vol. 23, no. 1, Art. no. 7, Jan. 2023, doi: 10.1186/s12911-023-02103-9.

120) A. Barredo Arrieta et al., "Explainable Artificial Intelligence (XAI): Concepts, taxonomies, opportunities and challenges toward responsible AI," Information Fusion, vol. 58, pp. 82–115, 2020.

121) J. Konecny et al., "Federated learning: Strategies for improving communication efficiency," *arXiv preprint*, arXiv: 1610.05492, 2016.

122) Y Schilder, Brian M et al. "Multi-omic insights into Parkinson's Disease: From genetic associations to functional mechanisms." Neurobiology of disease vol. 163 (2022): 105580. doi:10.1016/j.nbd.2021.105580.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

123) L. J. W. Evers et al., "Real-Life Gait Performance as a Digital Biomarker for Motor Fluctuations: The Parkinson@Home Validation Study," J. Med. Internet Res., vol. 22, no. 10, p. e19068, Oct. 2020.

124) Lian, Jie et al. "Personalized progression modelling and prediction in Parkinson's disease with a novel multi-modal graph approach." NPJ Parkinson's disease vol. 10,1 229. 1 Dec. 2024, doi:10.1038/s41531-024-00832-w.

125) C. Shorten and T. M. Khoshgoftaar, "A survey on image data augmentation for deep learning," *Journal of Big Data*, vol. 6, no. 1, p. 60, 2019.

126) C. G. Goetz et al., "Movement Disorder Society sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS)," Mov. Disord., vol. 23, no. 15, pp. 2129–2170, 2008.

127) Massano et al., "Clinical Approach to Parkinson's Disease: Features, Diagnosis, and Principles of Management," Cold Spring Harbor Perspectives in Medicine, 2012.

128) L. Memedi et al., "Automatic spiral analysis for objective assessment of motor symptoms in Parkinson's disease," Sensors, vol. 15, no. 9, pp. 23727–23744, 2015.

129) Postuma, Ronald B, and Daniela Berg. "Prodromal Parkinson's Disease: The Decade Past, the Decade to Come." Movement disorders : official journal of the Movement Disorder Society vol. 34,5 (2019): 665-675. doi:10.1002/mds.27670.

130) D. Weintraub and D. J. Burn, "Parkinson's disease: the quintessential neuropsychiatric disorder," Mov. Disord., vol. 26, no. 6, pp. 1022–1031, 2011.

131) Haehner, Antje et al. "Olfactory loss in Parkinson's disease." Parkinson's disease vol. 2011 (2011): 450939. doi:10.4061/2011/450939.

132) Postuma, Ronald B et al. "REM sleep behavior disorder: from dreams to neurodegeneration." Neurobiology of disease vol. 46,3 (2012): 553-8. doi:10.1016/j.nbd.2011.10.003.

133) Svenningsson, Per et al. "Cognitive impairment in patients with Parkinson's disease: diagnosis, biomarkers, and treatment." The Lancet. Neurology vol. 11,8 (2012): 697-707. doi:10.1016/S1474-4422(12)70152-7.

134) Schapira, Anthony H V et al. "Non-motor features of Parkinson disease." Nature reviews. Neuroscience vol. 18,7 (2017): 435-450. doi:10.1038/nrn.2017.62.

135) Prikrylova Vranova, Hana et al. "CSF markers of neurodegeneration in Parkinson's disease." Journal of neural transmission (Vienna, Austria : 1996) vol. 117,10 (2010): 1177-81. doi:10.1007/s00702-010-0462-z.

136) D. Brooks, "Imaging approaches to Parkinson disease," J. Nucl. Med., vol. 51, no. 4, pp. 596–609, 2010.

137) Feraco, Paola et al. "Imaging of Substantia Nigra in Parkinson's Disease: A Narrative Review." Brain sciences vol. 11,6 769. 9 Jun. 2021, doi:10.3390/brainsci11060769.

138) Tahmasian, Masoud et al. "Resting-state functional reorganization in Parkinson's disease: An activation likelihood estimation meta-analysis." Cortex; a journal devoted to the study of the nervous system and behavior vol. 92 (2017): 119-138. doi:10.1016/j.cortex.2017.03.016.

Volume 65 | Issue 06 | June 2026
DOI: 10.5281/zenodo.20642929

139) D. J. Brooks and N. Pavese, “Imaging biomarkers in Parkinson’s disease,” Prog. Neurobiol., vol. 95, no. 4, pp. 614–628, 2011, doi:10.1016/j.pneurobio.2011.08.009.

140) J. Politis, “Neuroimaging in Parkinson disease: From research setting to clinical practice,” Nat. Rev. Neurol., vol. 10, no. 12, pp. 708–722, 2014.

141) Waninger, Shani et al. “Neurophysiological Biomarkers of Parkinson's Disease.” Journal of Parkinson's disease vol. 10,2 (2020): 471-480. doi:10.3233/JPD-191844.

142) Zhang, Li et al. “A Survey on Deep Learning for Neuroimaging-Based Brain Disorder Analysis.” Frontiers in neuroscience vol. 14 779. 8 Oct. 2020, doi:10.3389/fnins.2020.00779.

143) S. Arora et al., “Detecting and monitoring the symptoms of Parkinson’s disease using smartphones: A pilot study,” Parkinsonism Relat. Disord., vol. 21, no. 6, pp. 650–653, Jun. 2015.

144) R. Z. U. Rehman, S. Del Din, Y. Guan, J. Q. Shi, A. J. Yarnall, and L. Rochester, "Selecting clinically relevant gait characteristics for classification of early Parkinson's disease: A comprehensive machine learning approach," Scientific Reports, vol. 9, art. no. 17269, Nov. 2019.